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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Christophe CAROLA et al.

Examiner: Yong Soo Chong

Serial No.: 10/667,653

Group Art Unit: 1617

Filed: September 23, 2003

Title: PREPARATION HAVING ANTIOXIDANT PROPERTIES

**BRIEF ON APPEAL UNDER 37 C.F.R. § 41.37**

Mail Stop - **Appeals**  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

This is an appeal from the decision of the Examiner finally rejecting claims 1-11 and 18 of the above-identified application.

**(1) REAL PARTY IN INTEREST**

The application is assigned of record to Merck Patent GmbH, who is the real party in interest herein.

**(2) RELATED APPEALS AND INTERFERENCES**

Appellants, their legal representative and the assignee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant appeal.

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### **(3) STATUS OF THE CLAIMS**

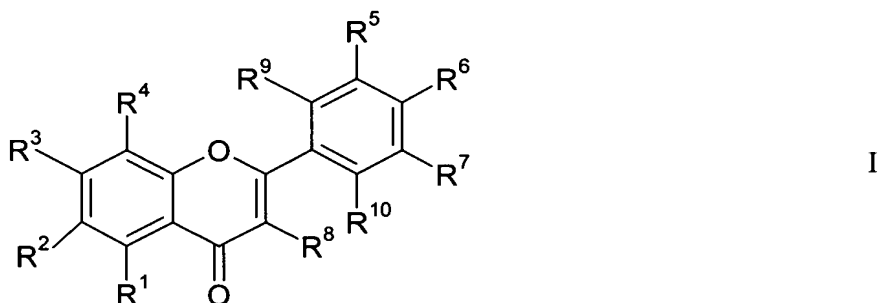
Claims rejected: Claims 1-11 and 18.  
Claims allowed: (none)  
Claims canceled: (none)  
Claims withdrawn: Claims 12-17.  
Claims on Appeal: Claims 1-11 and 18 (Copy of claims on appeal in attached Appendix).

### **(4) STATUS OF AMENDMENTS**

A Reply After Final Rejection containing claim amendments was filed on September 25, 2006, and was entered by the Examiner for the purposes of this appeal; see the Advisory Action mailed October 16, 2006. As a result, as noted in the Advisory Action, the previous objection to claim 5 is withdrawn and the rejection under 35 U.S.C. §112, first paragraph, is withdrawn.

### **(5) SUMMARY OF CLAIMED SUBJECT MATTER**

Appellants' invention (sole independent claim 1, on appeal) is directed to a composition for pharmaceutical or cosmetic application, or as a nutritional supplement, having antioxidant properties (see, e.g., page 1, paras. [0001] and [0002]; pages 5-16, para. [0012], first sentence; page 6, para. [0019]; and page 42, para. [0144]). The composition contains at least one compound of the formula I, which provides the antioxidant effect (see, e.g., pages 3-4, para. [0011]; and page 6, para. [0018]):



where the variables are as defined. The compound of formula I is contained in the compositions in an amount of from 0.01 to 20% by weight of such composition (see, e.g.,



page 6, para. [0020]).

**(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL**

The following sole outstanding ground of rejection is requested to be reviewed on appeal. Any separate consideration of the claims subject to this rejection are indicated.

1. The rejection of claims 1-11 and 18 under 35 U.S.C. §103, for allegedly being obvious from Ley (U.S. Patent No. 6,265,611) in view of Prendergast (WO 01/03681) and further in view of Jensen (U.S. Patent No. 2,550,255).

- a. Claims 1, 5-11 and 18, on appeal, are grouped together.
- b. Claims 2-4, on appeal, are separately grouped together for the reasons given in the argument.

**(7) ARGUMENT**

1a. Claims 1, 5-11 and 18, on appeal, are not obvious to one of ordinary skill in the art from Ley (U.S. Patent No. 6,265,611) in view of Prendergast (WO 01/03681) and further in view of Jensen (U.S. Patent No. 2,550,255), thus, the rejection of those claims under 35 U.S.C. §103 is not supported.

Ley teaches hydroxymandelic acid amides that have potent free radical scavenging and antioxidant properties (col. 2, lines 34-37). The compounds taught by Ley are monocyclic amides (see formula I at col.1), which are chemically distinct from the flavonoid compounds claimed by the instant invention. Ley neither discloses an antioxidant composition comprising flavonoid compounds nor any suggestion to one skilled in the art to substitute its monocyclic amides with the flavonoid compounds claimed by the instant application.

Prendergast discloses the use of a wide range of flavone, flavonone and related compounds as antiviral or anti-parasitic agents; see, e.g., page 1, lines 5-7, and pages 4-5. Prendergast provides no teaching or suggestion that these compounds have or would be expected to have antioxidant properties. See, e.g., the sections on "Applications" and "Enumerated embodiments" at pages 31-35, which, despite their broad scope, give no suggestion of an antioxidant effect for the flavone compounds of Prendergast. There is

no teaching or suggestion to one of ordinary skill in the art from Prendergast that its flavone compounds could be substituted for the monocyclic amides used as antioxidants in Ley

Jensen discloses a material useful in food products can be provided from the avocado plant *P. gratissima*, which is capable of inhibiting bacterial growth. Jensen describes only a preparation made from the ground up plant and identifies no particular compounds in the preparation. Jensen does not disclose the structure of any material which provides the antibiotic effect. Jensen also provides no hint that the material from the plant could contain a flavonoid compound of the instant invention. In fact, Jensen explicitly acknowledges that it is impossible to predict what compounds extracted and purified from the claimed plant material would have the desired biological effects (see col. 1, lines 26-33).

Appellants urge that there is no motivation to combine the reference teachings in a manner which suggests the instant claimed invention on appeal.

Of the three cited references, only Prendergast provides any suggestion of flavonoid compounds such as of appellants' formula I. However, Prendergast provides only a very broad generic teaching of flavone-type compounds. Formula 1 (page 4) of Prendergast generically encompasses the compounds of appellants' formula I but the reference gives no blazemarks to one of ordinary skill in the art to select the particular compounds used in the compositions of appellants' claim 1. The compounds of formula I of the instant claims have the particular structural feature that "at least 3 radicals from R<sup>1</sup> to R<sup>7</sup> are OH and that at least 2 pairs of -OH groups in the molecule are located at positions on a ring adjacent to one another, or R<sup>2</sup>, R<sup>5</sup> and R<sup>6</sup> are OH and the radicals R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>7-10</sup> are H." Although a few of the many specific compounds listed at pages 37-42 of Prendergast meet this requirement, the overwhelming majority do not. Prendergast gives no direction to one of ordinary skill in the art to select a compound meeting this requirement over its many other compounds encompassed. In any event, Prendergast gives no suggestion whatsoever to use such a compound in a composition having anti-oxidant properties. Prendergast also has no teaching or suggestion that such a compound should be provided in such a composition in an amount of 0.01 to 20% by

weight of the composition in order to provide an antioxidant effect.

No teachings from the cited art suggest to one of ordinary skill in the art that the Prendergast formula 1 compounds could be substituted in place of the hydroxymandelic acid amides of Ley to provide an anti-oxidant composition. To the contrary, Ley teaches one of ordinary skill in the art to use hydroxymandelic acid amides, which are monocyclic amides (see formula I at col.1), to provide an anti-oxidant effect. These monocyclic amides are completely chemically distinct from the flavone compounds of Prendergast (and from those of appellants' formula I).

Further, the very general disclosure in Ley that unspecified bactericides or fungicides can optionally be used in its compositions does not provide sufficient motivation to one of ordinary skill in the art to make the specific combination of the compounds of Prendergast's formula 1 into the Ley compositions. Ley's disclosure of optional further additives is a very broad shotgun-type recitation (col. 4, lines 25-39), i.e.:

The cosmetic and dermatological preparations according to the present invention can comprise cosmetic auxiliaries and additives, as are customarily-used in such preparations, e.g., preservatives, bactericides, fungicides, virucides, light filter substances, active ingredients with a cooling action, plant extracts, antiinflammatories, substances which promote wound healing, skin-lightening agents, skin-coloring agents, perfumes, antifoams, dyes, pigments which have a coloring action, thickeners, surface-active substances, emulsifiers, emollients, moisturizers and/or humectants, fats, oils, waxes or other customary constituents of a cosmetic or dermatological formulation, such as alcohols, polyols, polymers, foam stabilizers, electrolytes, organic solvents, silicone derivatives or chelating agents.

Such disclosure hardly provides one of ordinary skill in the art the necessary motivation to one of ordinary skill in the art to go to any reference which discloses any compound which may fall within these broad classes and select a specific such compound to combine in their compositions. The shotgun disclosure of Ley is far too remote to suggest to one of ordinary skill in the art use of any specific compound.

A suggestion to one of ordinary skill in the art to select a compound of Prendergast's formula 1 in view of such disclosure of Ley is made even further remote by the fact that Prendergast discloses bactericide or fungicide properties for its formula 1 compounds only a remote secondary property – as compared to the primary anti-viral or

anti-parasitic properties. The disclosure of these secondary properties in Prendergast (bottom of page 33) is, again, another shotgun-type disclosure lacking specificity. Even if one of ordinary skill in the art were motivated from Ley to pick out a specific bactericide or fungicide – from amongst all the other auxiliaries Ley broadly describes – one of ordinary skill in the art would not have been motivated to select a compound of Prendergast's formula 1 which discloses bactericidal and fungicidal properties only as secondary properties.

Furthermore, even if one of ordinary skill in the art were motivated to add a compound of Prendergast's formula I into the Ley compositions due to these remote recitations of optional agents, there is no motivation for one of ordinary skill in the art to select a flavone compound from Prendergast's broad genus which meets appellants' formula I. As discussed above, Prendergast gives no blazemarks for selection of a compound within its broad genus which meets the recitations of appellants' formula I.

The fact that each of Ley and Prendergast have remote teachings regarding bactericides and fungicides does not support the application of In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980), (cited at page 6, third and fourth paragraph, of the Final Office Action). In Kerkhoven, there were two references each teaching a specific set of compounds for the same specific property and thus it was found to be obvious that a combination of a specific compound from each reference would have the same specific property. The facts here are distinct. Ley does not disclose any particular compounds as a bactericide or fungicide. It merely provides a broad disclosure to use other additives in its compositions which might include unspecified bactericides or fungicides. This teaching fails to provide motivation to one of ordinary skill in the art to combine any particular bactericide or fungicide with the Prendergast compounds. Ley does not teach that the monocyclic amides disclosed therein are bactericides or fungicides, thus, there is no motivation under the Kerkhoven decision to combine such compounds with the flavones of Prendergast.

The combination of the teachings of Jensen add nothing to motivate using the Prendergast compounds in an anti-oxidant composition, such as that of Ley. Jensen admits that they do not even know what compounds are in its compositions for food

preservatives (see col. 1, lines 26-33). Thus, it provides no suggestion to one of ordinary skill in the art to use specific compounds within Prendergast's formula 1 in the compositions of Ley. Nor does Jensen provide any other teachings which are seen to apply in support of this ground of rejection.

Appellants respectfully submit that the only motivation for picking and choosing unrelated teachings from the three cited references comes from the impermissible use of appellant's own disclosure as a blueprint to reconstruct the claimed invention. Without appellant's own disclosure as a blueprint or guide, there is no direction in the art to combine the three cited references in a manner to arrive at appellant's invention or any suggestion of the desirability to do so. See Grain Processing v. American Maize, 5 USPQ2d 1788, 1792 (Fed. Cir. 1988); and Orthopedic Equipment Co., Inc. v. United States, 217 USPQ 193, 199 (Fed. Cir. 1983). No teachings – other than appellants' own disclosure – provides the necessary motivation to one skilled in the art to make the following selection and combinations of the reference teachings:

- modify the Ley compositions, directed to the use of monocyclic amides as anti-oxidants, to further add a bactericide or fungicide from amongst the broad and unspecified list of optional additives,
- select for such bactericide or fungicide a compound of Prendergast, even though Prendergast teaches the use of its flavone and related compounds for their anti-viral or anti-parasitic properties and only mentions bactericide or fungicide properties as some of several secondary properties, and
- select as such compound from Prendergast a specific compound included in only a small scope of its broad generic formula 1 which meets the particular requirements regarding OH groups recited for appellants' formula I.

There are no blazemarks provided from the reference teachings or objective basis for making all of these selections to reconstruct appellants' invention. Thus, there is insufficient motivation to combine the references in this manner.

Additionally, appellants submit that each of the Ley, Prendergast and Jensen references are directed to diverse and nonanalogous art areas and to inventions directed to

solving distinct problems. The case law regarding non-analogous art, thus, further supports an absence of motivation to combine these teachings in the manner alleged in the Final Office Action. The two-step test for non-analogous art is set forth in In re Clay, 966 F.2d 656, 23 USPQ2d, 1058 (Fed. Cir. 1992). The first step inquires as to whether the references are in the same field of endeavor. In the present situation, they are not. As noted above, Ley discloses compounds for free-radical scavenging effects, Prendergast discloses structurally very distinct compounds primarily for antiviral and/or anti-parasitic effects, and Jensen discloses unidentified compounds as antibiotics. These are diverse fields of endeavor. The second step is to inquire whether the references are "reasonably pertinent to the same problem." Again, the problems are not the same. The problem in Ley was to find a compounds for anti-oxidant effects, the problem in Prendergast was to find an anti-viral or anti-parasitic compound and the problem in Jensen was to find a food-friendly antibiotic. Thus, it is urged that the cited references are in non-analogous areas and, therefore, lack of motivation is further shown.

Appellants respectfully submit that the allegation in the Final Office Action (p. 5, fourth paragraph) that appellants' previous reply was insufficient because it merely attacked the references individually is not an accurate reflection of appellants' arguments in the prosecution. Appellants clearly addressed why one of ordinary skill in the art would not have been motivated to combine the reference teachings in a manner supporting the rejection. Those were essentially the same reasons as provided above in this Brief. The Final Office Action (p. 6, second paragraph) even noted that appellants made such arguments. Appellants are not barred from also discussing what the individual references teach and such additional discussion does not make their argument incorrect or less convincing. To the contrary, the individual teachings of the references must be considered to know whether there is motivation to combine them and, if combinable, what such combination would suggest. Appellants did clearly address the combined teachings of the prior art and, accordingly, the Keller and Merck & Co. case law cited on page 5 of the Final Office Action cannot be relied upon to discount appellants' arguments.

For all of the above reasons, it is urged that consideration of Ley, Prendergast and Jensen, as a whole, does not render the invention of claims 1, 5-11 and 18, on appeal,



obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 is not supported and should be reversed.

1b. Claims 2-4, on appeal, are not obvious to one of ordinary skill in the art from Ley (U.S. Patent No. 6,265,611) in view of Prendergast (WO 01/03681) and further in view of Jensen (U.S. Patent No. 2,550,255), thus, the rejection of those claims under 35 U.S.C. §103 is not supported.

The arguments made above in Issue 1a. apply equally to these claims on appeal and are incorporated herein by reference. An additional basis for patentability applies to claims 2-4, on appeal.

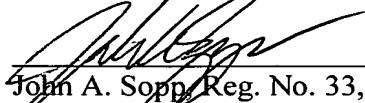
Claims 2-4 are directed to compositions with even more specifically defined compounds of appellants' formula I. Although appellants believe, for the reasons stated above, that there is no motivation to select from Prendergast the compounds of formula I in claim 1, on appeal, there is even less basis for one of ordinary skill in the art to select the even more particularly defined compounds of claims 2-4, on appeal.

For these reasons, it is urged that consideration of Ley, Prendergast and Jensen, as a whole, does not render the invention of claims 2-4, on appeal, obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 is not supported and should be reversed.

For all of the above reasons, it is urged that the decision of the Examiner rejecting claims 1-11 and 18, on appeal, is in error and should be reversed.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

  
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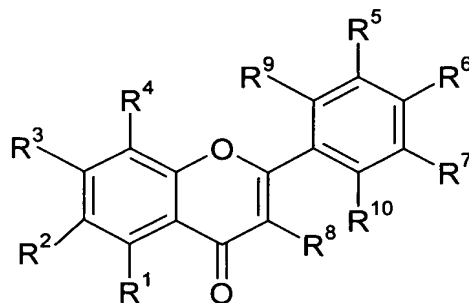
Attorney Docket No.: MERCK-2753

Date: December 26, 2006

JAS:blb

## CLAIMS APPENDIX

1. A composition for pharmaceutical or cosmetic application, or as a nutritional supplement having antioxidant properties comprising at least one compound of the formula I in an amount of from 0.01 to 20% by weight of such composition



I

where R<sup>1</sup> to R<sup>10</sup> may be identical or different and are selected from

- H
- OR<sup>11</sup>
- a straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkyl group,
- a straight-chain or branched C<sub>3</sub>- to C<sub>20</sub>-alkenyl group,
- a straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-hydroxyalkyl group, where the hydroxyl group is bonded to a primary or secondary carbon atom of the alkyl group and wherein the alkyl group is optionally interrupted by oxygen, and/or
- a C<sub>3</sub>- to C<sub>10</sub>-cycloalkyl group, or a C<sub>3</sub>- to C<sub>12</sub>-cycloalkenyl group, where the rings are each optionally bridged by -(CH<sub>2</sub>)<sub>n</sub>- group, where n = 1 to 3,
- where OR<sup>11</sup> is, independently of one another,
  - OH
  - a straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-alkoxy group,
  - a straight-chain or branched C<sub>3</sub>- to C<sub>20</sub>-alkenyloxy group,
  - a straight-chain or branched C<sub>1</sub>- to C<sub>20</sub>-hydroxyalkoxy group, where the hydroxyl group is bonded to a primary or secondary carbon atom of the chain and furthermore the alkyl chain is optionally interrupted by oxygen,
  - a C<sub>3</sub>- to C<sub>10</sub>-cycloalkoxy group, or a C<sub>3</sub>- to C<sub>12</sub>-cycloalkenyloxy group, where

- the rings are each optionally bridged by  $-(CH_2)_n-$  group, where  $n = 1$  to  $3$ ,
- a mono- and/or oligoglycosyl radicals,
- with the proviso that:
- at least 3 radicals from  $R^1$  to  $R^7$  are OH and that at least 2 pairs of -OH groups in the molecule are located at positions on a ring adjacent to one another, or  $R^2$ ,  $R^5$  and  $R^6$  are OH and the radicals  $R^1$ ,  $R^3$ ,  $R^4$  and  $R^{7-10}$  are H.
2. A composition of claim 1, comprising at least one compound of the formula I wherein radicals  $R^1$  to  $R^4$  and radicals  $R^5$  to  $R^7$  each comprise at least two -OH groups located at positions on a ring adjacent to one another.
  3. A composition of claim 1, comprising at least one compound of the formula I wherein radicals  $R^1$  to  $R^4$  comprise at least three -OH groups located at positions on a ring adjacent to one another.
  4. A composition of claim 1, comprising at least one compound of the formula I wherein the radicals  $R^1$  to  $R^3$  are OH.
  5. A composition of claim 1, comprising one or more compounds of the formula I in an amount of from 1 to 8% by weight.
  6. A composition of claim 1, comprising one or more compounds of the formula I in an amount of from 0.1 to 10% by weight.
  7. A composition of claim 1, for the protection of body cells against oxidative stress, further comprising one or more other antioxidants and/or vitamins.

8. A composition of claim 7, wherein said anti-oxidant or vitamin is vitamin A palmitate, vitamin C or a derivative thereof, DL- $\alpha$ -tocopherol, tocopherol E acetate, nicotinic acid, pantothenic acid or biotin.
9. A composition of claim 1, further comprising one or more UV filters.
10. A composition of claim 9, wherein said UV filter is 3-(4'-methylbenzylidene)-dl-camphor, 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl)propane-1,3-dione, 4-isopropyl-dibenzoylmethane, 2-hydroxy-4-methoxybenzophenone, octyl methoxycinnamate, 3,3,5-trimethylcyclohexyl salicylate, 2-ethylhexyl 4-(dimethylamino)benzoate, 2-ethylhexyl 2-cyano-3,3-diphenylacrylate, or 2-phenylbenzimidazole-5-sulfonic acid and its potassium, sodium and triethanolamine salts.
11. A composition of claim 1, said composition being a food or a food supplement and further comprising an excipient which is suitable for a food or a food supplement.
18. A composition of claim 1, which is in the form of an emulsion.

**EVIDENCE APPENDIX**

(none)

**RELATED PROCEEDINGS APPENDIX**

(None)